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Immunophenotyping of Myelodysplasia

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Abstract

As the incidence of myelodysplastic syndromes (MDS) increases with the ageing of the population, new and promising therapeutic approaches are being developed. "Proper application of such new strategies relies on a thorough diagnosis of these variable and pleiomorphic disorders. Cytology and cytogenetics are included in the stratification of MDS, and are the main classification criteria in two successive systems. However, the progress of multiparametric immunophenotyping and flow cytometry techniques suggest that this approach may soon become an inclusive part of the diagnostic criteria of MDS. In this review of the literature, the features of MDS and the evolution of the classification these disorders is first summarized. An extensive analysis of flow cytometry approaches, especially multiparametric, is then presented, comparing the various strategies and their output.

Current information regarding immunophenotyping of MDS indicates that several anomalies in the expression of leukocyte differentiation antigens are invaluable for their diagnosis and prognosis. A more thorough and standardized comparison between normal bone marrow and MDS samples, including pattern evaluation rather than as subset enumeration, should soon further provide an efficient tool for the definition and outcome prediction of these diseases. The diagnosis of myelodysplastic disorders (MDS) currently relies on cytological features and karyotypic anomalies. These methods allow using current classifications to discriminate between the various forms of MDS. A review of the literature demonstrates that the past 5 years have seen increasing information regarding multiparametric

Abbreviations: MDS, Myelodysplastic syndromes; FAB, French-American British classification; WHO, World Health Organization; RA, Refractory Anemia; RARS, Refractory Anemia with Ringed Sideroblasts; RAEB, Refractory Anemia with Excess of Blasts; RAEB-t, Refractory Anemia with Excess Blasts in Transformation and CMML; Chronic MyeloMonocytic Leukemia, IPSS; International Prognosis Scoring System.

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immunophenotyping of MDS bone marrow by flow cytometry. These approaches, once standardized, should provide an additional valuable tool for the diagnosis and management of MDS patients.

Keywords: Myelodysplastic syndrome; Immunophenotype; flow cytometry; WHO classification; FAB classification

1. Introduction

Among malignant hematological diseases, myelodysplasia, or more precisely, myelodysplastic syndromes (MDS) are one of the most frequent clonal disorders of the bone marrow in elderly people, yet may develop at any age. The incidence of MDS is evaluated as 1–2/100,000 population per year [1–4]. This incidence has been reported to increase up to 30 cases per 100,000 population per year in patients over 70 years old [2]. The recent improvement of life expectancy may explain the fact that more and more cases appear to be diagnosed [5].

Myelodysplastic syndromes are clonal diseases in which a hyperproliferative process is counterbalanced by massive intramedullary apoptosis [6]. Clonal evidence has been demonstrated quite early [7] but the identity of the cell in which transformation takes place is more difficult to determine and although it is likely to be a stem cell, this is still debated [8,9]. Indeed, severe hematopoietic alterations exist both at the level of hematopoietic progenitors and their microenvironment [10]. Moreover, the apoptotic cascade appears to be altered and uncontrolled in MDS [11,12].

As a result of such complex biological processes, three different compartments coexist in MDS bone marrow: residual normal hematopoiesis, monoclonal proliferative cells and pre-leukemic/leukemic blasts. The latter are characterized by differentiation arrest and grow progressively as MDS evolves through acute transformation. Indeed, the major complication of MDS is the development of acute leukemia and/or the worsening of cytopenia. However, the treatment of MDS has long consisted only of supportive transfusion therapies, and it is only recently that a better understanding of the natural history of MDS and the discovery of molecular abnormalities led to increasingly successful therapeutic trials. These therapeutic approaches include the availability of recombinant hemopoietic growth and angiogenic factors, the design of inhibitors of tyrosine kinase and other enzymes, and even the use of immunomodulators [reviewed in 13].

The proper application of these new therapies requires a correct and detailed diagnosis. As in malignant hematological disorders, the diagnosis of MDS combines cytological, cytogenetic and more recently immunophenotypic investigations.

This review will focus on the development of these immunophenotypic approaches, not yet standardized but extremely promising as a complementary tool for the definition of MDS and also providing a number of prognostic factors. After a definition of MDS, the immunophenotypic features of these disorders reported to date will be summarized and currently identified immunophenotypic prognostic factors described.

2. Definition of MDS

Myelodysplastic syndromes are a heterogeneous group of disorders characterized by ineffective hematopoiesis, translating into peripheral cytopenia of one, two or three lineages,